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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,774	04/02/2004	Shotaro Yamaguchi	Q80844	1205

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SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, NW
Washington, DC 20037-3213

EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,774	YAMAGUCHI, SHOTARO	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/727,769.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-2-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 26-39 are currently pending and are present for examination. Original claims 1-25 have been cancelled by the applicants in the preliminary amendment filed on 4-2-04.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 4-2-04 has been considered by the examiner.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

Examiner notes that applicants have not updated the relationship of the instant application to its parent application that has matured in to a US patent. Examiner urges applicants to amend said information by providing the US patent number in response to this Office action.

Claim Objections

Claims 36-38 are objected to because of the following informalities: Claims 36-38 fail to recite biological names in italics. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26-30, and 39 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 26-30 and 39 are drawn to "an enzyme..." and "a composition..." which reads on a product of nature. Claims directed to products of nature are considered to comprise non-statutory subject matter. Examiner suggests amending the claims to recite "An isolated polypeptide.." to show the hand of man and thus overcome the above rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 28 recites the phrase "derived from a microorganism". The metes and bounds of this phrase are not clear to the Examiner. Literally, while the term "derived" means "to isolate from or obtain from a source", the above term could also mean "to arrive at by reasoning i.e., to deduce or infer" or also mean "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the "derived from a microorganism" encompasses specific enzymes as in "isolated from a microorganism" or whether it

encompasses recombinants, variants and mutants from any source and labeled as "derived from a microorganism". As applicants have not provided a definition for the above phrase, Examiner has interpreted the phrase broadly to mean, said enzyme encompasses sequences, which are recombinants, variants, or mutants of any deamidase from any source. Examiner has given the same interpretation while considering the claims for all other rejections.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 31 recites the phrase "has homology with". The metes and bounds of this phrase in the context of the claim are not clear to the Examiner. It is not clear as to what percent homology is encompassed in this phrase. A perusal of the specification did not provide the Examiner with a definition.

Claims 32-33 and claims 34-38 depending therefrom are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 32- 33 recite the phrase "a novel enzyme". This phrase constitutes an opinion by applicant on the merits of the claim and is therefore not considered proper. Deletion of the word novel is suggested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-29, 31-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide or a composition comprising SEQ ID NO:6 encoded by the polynucleotide with SEQ ID NO:5 wherein the polypeptide is an enzyme, which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, and a method for producing said polypeptide by culturing a transformed cell, transformed with a vector comprising the polynucleotide encoding the amino acid sequence SEQ ID NO:6 does not reasonably provide enablement for such any or all such polypeptide including variants, mutants and recombinants isolated from any or all sources or including variants, mutants and recombinants of SEQ ID NO:6 wherein one or more of amino acid residues of the amino acid sequence may be modified by at least one of deletion, addition, insertion and substitution. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 26-29, 31-39 are so broad as to encompass any deamidating enzyme from any or all sources including variants, mutants and recombinants of SEQ ID NO:6. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the

extremely large number of enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only single specific deamidase having an amino acid sequence SEQ ID NO:6. It would require undue experimentation of the skilled artisan to make and use the polypeptides as claimed. The specification is limited to teaching the SEQ ID NO: 6 as the specific enzyme but provides no guidance with regard to the making of variants and mutants of SEQ ID NO:6 or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the polypeptides for use in the claimed method, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success

in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompasses any or all deamidating enzymes including polypeptides comprising all modifications and fragments of SEQ ID NOS:6 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting deamidating activity; (B) the general tolerance of said deamidases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on the polypeptide SEQ ID NO:6 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with an enormous number of amino acid modifications in SEQ ID NOS: 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics for use in the claimed method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 26-29, 32-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 26-29, 32-39 are directed to any or all polypeptides having deamidase activity and polypeptides and fragments corresponding to the sequence of SEQ ID NO:6 and variants, mutants and recombinants of SEQ ID NO:6 as well as method of making said polypeptide using transformed cells. Claims 26-29, 32-39 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:6 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:6 and fragments of SEQ ID NO:6 that have not been disclosed in the specification as well as method of making said polypeptides using transformed cells. No description has been provided of all the sequence encompassed or the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:6 has been provided by applicants, which would indicate that they had possession of the genus of modified polypeptides or a method of making the same. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:6, including fragments and variants within the scope of the genus of polypeptides to be used in the claimed method. The genus of polypeptides required for the claimed method is a large variable genus including peptides, which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the

scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 38 is rejected because the invention appears to employ a novel *Chryseobacterium* microorganism. Since the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed microorganism is not fully disclosed, nor has been shown to be publicly known and freely available. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public. Accordingly, it is deemed that a deposit of the microorganism should have been made in accordance with 37 CFR 1.801-1.809. In order for the claims to be enabled, applicants must show that either the microorganism can be made by publicly available materials or that the microorganism as such has been deposited in such a way that it is freely available to the public. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the microorganism. It appears that applicant has made a deposit. However, its public availability is not clear.

The deposit can be made in a recognized Biological Deposit Center. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific plasmid/strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-27, 29-30, 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Vaintraub et al. (FEBS Lett. 1992, Vol. 302(2):169-171, cited in the IDS). This rejection is based upon the public availability of a printed publication. Claims 26-27, 29-30, 39 of the instant application are drawn to a polypeptide, which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides.

Vaintraub et al. disclose such a deamidase to deamidate the amido groups from a protein. Examiner is aware that the reference does not specifically disclose that said enzyme is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides. However, it must be recognized that the reference also does not specifically disclose that said enzyme does not have the above characteristic. In view of the above reasoning Examiner takes the position that the reference enzyme and the enzyme claimed are one and the same and therefore Vaintraub et al. anticipate claims 26-27, 29-30, 39. Examiner is also aware that the reference does not disclose a specific amino a cid sequence for the enzyme as opposed to the enzyme claimed in claim 30. However, Examiner takes the position that a characteristic such as the amino acid sequence of a protein is its inherent characteristic and because the polypeptide in the reference has the same function as that claimed herein, Examiner takes the position that the reference enzyme indeed inherently has the same amino acid sequence as that of the polypeptide claimed herein.

Claims 26-27, 29-30, 32-33, 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Vinogradov et al. (Prikladnaya Biokhimiya i Mikrobiologiya (1976), 12(5), 704-8). This rejection is based upon the public availability of a printed publication. Claims 26-27, 29, 32-33, 39 of the instant application are drawn to a polypeptide, which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, wherein said polypeptide is isolated from a microbial source and a method of making said polypeptide by culturing the microorganism in a medium and extracting the enzyme from said culture.

Vinogradov et al. disclose such a deamidase to deamidate the amido groups from a protein isolated from a microbial source and wherein said enzyme is prepared by culturing the bacterial culture producing the same. Examiner is aware that the reference does not specifically disclose that said enzyme is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides. However, it must be recognized that the reference also does not specifically disclose that said enzyme does not have the above characteristic. In view of the above reasoning Examiner takes the position that the reference enzyme and the enzyme claimed are one and the same and therefore Vinogradov et al. anticipate claims 26-27, 29-30, 32-33, 39. Examiner is also aware that the reference does not disclose a specific amino a cid sequence for the enzyme as opposed to the enzyme claimed in claim 30. However, Examiner takes the position that a characteristic such as the amino acid sequence of a protein is its inherent characteristic and because the polypeptide in the reference has the same function as that claimed

herein, Examiner takes the position that the reference enzyme indeed inherently has the same amino acid sequence as that of the polypeptide claimed herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vaintraub et al. and Sambrook et al. (Molecular Cloning, A Laboratory Manual, 2nd Ed, ColdSpring Harbor Laboratory Press, 1989, pages 7.37-7.52). Claim 31 is drawn to a recombinant deamidase obtained by culturing a transformed cell, transformed with a vector comprising a polynucleotide encoding a deamidase which is capable of deamidating amido groups in target proteins and peptides by directly acting upon said amido groups without cutting peptide bonds and without cross-linking said target proteins or peptides, wherein said polypeptide either has the amino acid sequence SEQ ID NO:6 or is a mutant, or variant of SEQ ID NO:6.

The reference of Vaintraub et al., teaches a deamidase which the Examiner argues as inherently being the same as that claimed in this application. However, while the reference teaches the method of isolating, purifying and characterizing the enzyme the reference does not teach a recombinant enzyme.

Sambrook et al. teach exhaustive methods of making recombinant protein starting from a purified protein, which has been used by a number of inventors to arrive at recombinant protein

starting from a purified protein. Therefore combining the teachings of the above two references, it would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of Vaintraub et al. et al. with that of Sambrook et al. to arrive at a recombinant protein. One of ordinary skill in the art would be motivated to do this in order to prepare large amounts of the protein. One would have a reasonable expectation of success since Vaintraub et al. provide the purified protein and Sambrook et al. teach a reliable and time-tested method that has been used by a number of other inventors.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

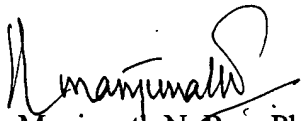
A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 26-28, 30-31, 39 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3 of prior U.S. Patent No. 6,251,651. This is a double patenting rejection.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652
September 29, 2006